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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,796	06/07/2001	Kathleen L. Horwath	RB-125 SEQ	9032

7590 10/18/2005

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EXAMINER	
ROBINSON, HOPE A	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 10/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/876,796	HORWATH ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-38* is/are pending in the application.

4a) Of the above claim(s) *38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to comply*.

DETAILED ACTION

Application Status

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

2. Applicant's response to the Office Action mailed February 16, 2005 on July 20, 2005, is acknowledged.

Claim Disposition

3. Claims 1-26 and 39-40 have been canceled. Claims 27-38 are pending. Claims 27-37 are under examination.

Information Disclosure Statement

4. The Information Disclosure Statement filed on July 27, 2005 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

Withdrawn-Specification Objections

5. Previous objection to the specification are withdrawn by virtue of submission of an amendment.

Withdrawn- Abstract Objections

6. Previous objection to the Abstract is withdrawn by virtue of submission of an amendment.

New-Specification

7. The specification is objected to because of the following informalities:

The specification is objected to because the paragraph on page 22, line 16 has been amended to disclose "SEQ ID NO:2-4 pertaining to Fig. 2.6, however, it is unclear which sequence corresponds to for example Fig 2.6c or 2.6a or 2.6b. The corresponding sequence identifiers need to be aligned with the specific figures that display them.

Correction is required.

Maintained-Drawing Objection

8. As previously stated, the drawings are objected to because Figure 4.3 has the following labels that are inconsistent, "A. and B", which should be "A. and B.". Note that Figures 2.6a-c for example disclose sequences, however, the specification describes Fig 2.6 as having the disclosed structures. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the

sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

New-Sequence Compliance Objection

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR1.821 through 1.825; applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicant is required to identify all amino acid sequences of at least 4 L-amino acids and at least 10 nucleotides by a sequence identifier, i.e., "SEQ ID NO:". The specification discloses sequences that have not been identified by a sequence identifier, see for example, page 9 where SEQ ID NO:785071 is disclosed. If these sequences have not been disclosed in the computer readable form of the sequence listing and the paper copy thereof, applicant must provide a computer readable form of the "Sequence Listing"

including these sequences, a paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable form copies are the same and, where applicable, include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See the attached Notice to Comply with the sequence rules.

New-Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 27-37 are rejected under 35 U.S.C. 101 because the claimed invention includes non-statutory subject matter. The claimed invention is directed to a method for providing antifreeze or recrystallization inhibition properties to a subject formulation comprising the use of an activated polypeptide. In addition, said method can be used to create transgenic or gene-modified plants, crops, fish or animals having greater tolerance to cold climatization, in particular transgenic humans. Further, applicant has stated on the record on page 29-30 of the amendment filed on July 20, 2005 that the claimed method is intended to be used to create transgenic human beings that have greater tolerance for cold climates. Therefore, the claimed invention includes non-statutory subject matter. It is suggested the claims are rewritten to exclude human beings.

Amended and Maintained-Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 27-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for providing antifreeze or recrystallization inhibition properties to a subject formulation, does not reasonably provide enablement for said method wherein the polynucleotides for the activated protein are used to create transgenic or gene-modified plants, crops, fish or animals having greater tolerance to cold climatization. The specification is not enabled for all transgenic cells and organisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth

of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass a human being or other mammals/whole organisms that are not supported by the instant specification. The claim encompasses the creation of a transgenic organism or animal or mammal including a human being having a greater tolerance to cold climatization via gene therapy methods. The instant specification and the art generally provides support for fish, plants, foods for example, however, does not provide support for creating a human being that has a greater resistance to cold climatization. There is no demonstration or evidence provided in the instant specification to transgenically create such a human. The instant specification and claims disclose transgenic cells and organisms, which reads on an *in vivo* environment. The disclosed transgenic cells/organisms/animals reads on a whole animal and therefore a human being, and the instant claim 37 is not enabled for the full scope. In view of the foregoing, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims.

Predictability of the success of creating a whole organism/animal such as a human being that has a greater tolerance for cold climates is not supported by the art or the instant specification.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. For example, Eliot (Science, vol. 269 (5227), pages 1050-55, 1995) indicates that gene therapy has more than 100 clinical trials with millions of dollars invested, however is struggling to meet the expectations and that a product realistically is far off. The Eliot reference

indicates that while there is support for gene therapy and several reports of gene transfer and expression there is still little or no evidence of therapeutic benefits in patients or even in animal models (page 1050). As there is no analogous art, the specification needs to provide adequate guidance/direction to enable the skilled artisan to practice the claimed invention commensurate in scope with the claims.

The working examples provided do not rectify the missing information in the instant specification as the claims broadly read on a human being which is neither exemplified in the specification or the prior art. Thus, one of skill in the art would have to engage in undue experimentation to practice the claimed invention commensurate in scope with the claims.

The issue in this case is the breath of the claim in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, for all these reasons the claimed invention is not enabled to the full extent of the claimed scope.

Withdrawn-Claim Rejections - 35 USC ∋ 112

12. Previous rejection to claims regarding indefiniteness is withdrawn by virtue of submission of an amendment that inserted the term "obtain" in claim 27.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 27-28, 31 and 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Rubinsky et al. (U.S. Patent No. 5,358,931, October 25, 1994).

Rubinsky et al. teach methods of formulation and use of thermal hysteresis proteins that offer benefits by imparting the preservation and improved viability of cell suspensions, tissues and whole organs by achieving antifreeze properties (see abstract and column 2), said proteins in concentrations of 1mg/mL or more (claim 27, see column 10). Rubinsky et al. disclose freezing point depression in a non-colligative manner and antifreeze specific inhibition (claim 28, see columns 2-3). The method of Rubinsky et al. is directed to plant cells, plant seeds and whole plants (claim 31, column 4 of the patent). In addition, Rubinsky et al. teach cryopreservation of target tissues (column 5) and hypothermic exposure (claim 33, see column 14). Claim 34 is anticipated because Rubinsky et al. teach a method that protects the cell or a whole organism such as a plant (claim 35) under adverse conditions such as the formation of ice crystals (claim 34), see columns 3-4. Rubinsky et al. disclose that their invention has application in the

preservation of foods, which would otherwise lose their appeal due to the breakdown of cell structures and functions in the foodstuffs (claim 36, column 4). Therefore the limitations of the claims are met by the reference.

Response to Arguments

14. The response filed on July 20, 2005 has been considered, however, is not fully persuasive. Note that formal issues remain pertaining to the specification, drawings and sequence compliance for the reasons stated above and because applicant did not address all issues raised. The response on page 28 state that "applicant retain the right to present claims 1-26, 38 and 39-40 in a divisional application", note however, that claim 38 is still pending in the instant application.

The rejection of record under 35 U.S.C. 112, first paragraph over claim 37 remains and has been amended to include claims 27-36 based on applicant's statement on the record as to how the claimed invention should be interpreted. Applicant on pages 29-30 argues that it is possible to create transgenic human cells and that the predictability of the success of creating a whole organism/animal such as a human being, that has greater tolerance for cold climates is supported by Cavazzanna-Calvo. Applicant points to references such as Cavazzanna-Calvo for support of arguments in favor of gene therapy, however, the art generally recognizes that said therapy is unpredictable. Applicant is reminded that the creation of whole organisms such as human beings is non-statutory subject matter. However, it is noted that the instant specification does not provide support for such an invention. Therefore the claimed invention is rejected as the instant

specification is not enabled for the full scope of the claims. There is no demonstration in the disclosure of the phenotypic changes claimed and the claims broadly read on humans, which is not supported by the disclosure and represents non-statutory subject matter. There is no demonstration in a plant for example, of said phenotypic change. It is suggested that applicant cancel claim 37 or amend the claims to recite non-human animals. In addition, based on applicant's arguments a new ground of rejection has been instituted under 35 U.S.C. 101, as applicant has stated on the record the intent to use the claimed invention to create whole organisms including human beings.

Furthermore, the rejection under 35 U.S.C. 102 remains, however is amended. The response on page 31 states that Rubinsky et al. differs from the claimed invention in that the reference pertains to AFP and the claimed invention pertains to TmAFP. This argument is not persuasive as the limitations of the specification cannot be read into the claims. The claims do not recite such a derivation, thus can be obtained from any source since none is claimed. Applicant further provides specific characteristics of TmAFP, however, value is being placed on a limitation that is not present in the claims. Thus, the rejections remain.

Conclusion

15. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 10/13/05

HOPE ROBINSON
PATENT EXAMINER

Application No.: 09/876,796

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

[x] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

[ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

[ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

[x] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

[x] 7. Other: Additional sequence in specification

8. **Applicant Must Provide:**

[x] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

[x] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[x] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g).

For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
- For CRF Submission Help, call (703) 308-4212
- For PatentIn software Program Support:
  - HELP DESK: (703) 739-8559, ext 508, M-F, 8 AM to 5 PM EST except holidays
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